Noninvasive de novo imaging of human embryonic stem cell-derived teratoma formation.

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Public Summary:

Scientific Abstract:
Teratoma formation can be a serious drawback after the therapeutic transplantation of human embryonic stem (hES) cells. Therefore, noninvasive imaging of teratomas could be a valuable tool for monitoring patients undergoing hES cell treatment. Here, we investigated the angiogenic process within teratomas derived from hES cells and now report the first example of using (64)Cu-labeled RGD tetramer ((64)Cu-DOTA-RGD4) for positron emission tomography imaging of teratoma formation by targeting alpha(v)beta(3) integrin. H9 hES cells (2 x 10(6)), stably expressing firefly luciferase, and enhanced green fluorescence protein (Fluc-eGFP) were injected into adult nude mice (n=12) s.c. Eight weeks after transplantation, these hES cell grafts evolved into teratomas as confirmed by longitudinal bioluminescence imaging. Under micropositron emission tomography imaging, 2-deoxy-2-[(18)F]fluoro-D-glucose and 3'-deoxy-3'-[(18)F]-fluorothymidine both failed to detect hES cell-derived teratomas (0.8+/-0.5 versus 1.1+/-0.4 %ID/g, respectively; P=not significant versus background signals). By contrast, (64)Cu-DOTA-RGD4 revealed specific and prominent uptake in vascularized teratoma and significantly lower uptake in control tumors (human ovarian carcinoma 2008 cell line), which had low integrin expression (10.1+/-3.4 versus 1.4+/-1.2 %ID/g; P<0.01). Immunofluorescence staining of CD31 and beta(3) integrin also supported our in vivo imaging results (P<0.05). Moreover, we found that the cells dissociated from teratomas showed higher alpha(v)beta(3) integrin expression than the 2008 cells. In conclusion, by targeting alpha(v)beta(3) integrin, we successfully showed the ability of (64)Cu-DOTA-RGD4 to noninvasively visualize teratoma formation in vivo for the first time.